While the WOMAC pain and physical function scores indicated a mild to moderate level of pain and disability over the past 48 hours, prospective data collection (Participant Diary) detected higher levels of knee pain when the highest score reported of the 7 day period was utilized (highest 7-day knee pain). Further, the prospective 7-day Participant Diary also demonstrated almost half of the study participants (44%) with a mean global assessment of their knees as only 'fair' or 'poor'.
A simple Participant Diary requiring daily recording of knee pain specified as 'at its worst' on a 11 point rating scale over one week may provide an inexpensive, robust and responsive outcome measure in long term clinical trials compared to retrospective reporting of pain (past 48 hours) but without descriptive specificity.

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VALIDATION OF DIGITALIZED HEALTH STATUS QUESTIONNAIRES FREQUENTLY USED IN THE MONITORING OF OSTEOARTHRITIS: A CROSS SECTIONAL STUDY

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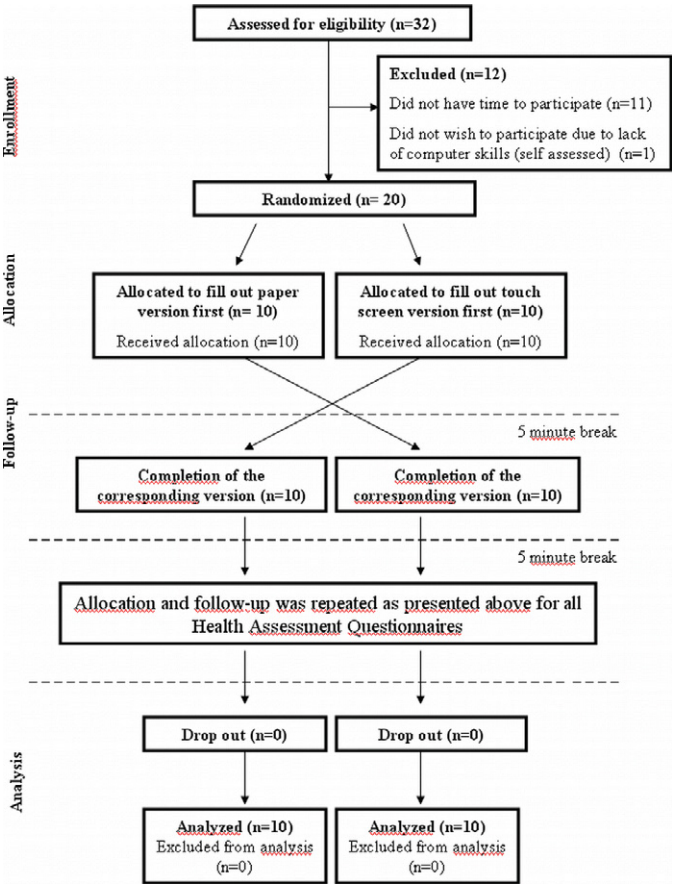
Purpose: To validate digitalized Health Status Questionnaires (HSQs) used for sampling Patient Reported Outcomes for knee osteoarthritis (KOA) patients, employing newly developed freeware on touch screens. Furthermore to examine the effect of patient characteristics on differences between HSQ-versions.
Methods: Touch screen answers were compared to answers on paper versions of the most commonly used HSQs in the clinical management of KOA, and participants were recruited from an ongoing in-house KOA trial (the CAROT-study; ClinicalTrials.Gov Identifier: NCT00655941). 20 female participants, mean age 67 (SD 7), completed KOOS, SF-36, ADL Taxonomy, Physical Activity Scale, VAS pain, function and patient global and Pain Detect, and the trial profile ensured testing of only one HSQ at the time in a repeated randomized cross-over design. The two HSQ versions (paper and touch screen) were completed with a 5 min. interval and between each HSQ patients had a 5 min. break. Mean values for each version, mean differences (95% CI), pooled means, medians, median differences, Minimal Important Differences and Spearman correlation coefficients were calculated for all HSQs including relevant subscales.
Results: Correlations between touch screen and paper version of SF-36 were 0.92 for the physical component summary scale and 0.81 for the mental component summary scale. Similar correlations for KOOS ranged from 0.88 to 0.98, and the other instruments were tested with comparable results. When analysing mean and median differences we found no consistent pattern in differences between the two measures, nor were there any systematic patterns in the differences between HSQ-versions. No significant influence was observed of age, former computer experience or level of education on differences between the two HSQ-versions. The participants did not need further help or explanations when filling out questionnaires on screen and found the process easier than filling in paper versions of the questionnaire. 16 of 20 overall preferred the touch screen version.



Correlation between paper- and touch-screen versions

Paper version	Spearmans Correlation Coefficient	Touch Screen Version
KOOS	0.97	KOOS
VAS pain	0.89	VAS pain
VAS function	0.87	VAS function
VAS patient global	0.78	VAS patient global
SF-36$_{\text{Physical Component Summary Scale}}$	0.92	SF-36$_{\text{Physical Component Summary Scale}}$
SF-36$_{\text{Mental Component Summary Scale}}$	0.81	SF-36$_{\text{Mental Component Summary Scale}}$
Physical Activity Scale	0.84	Physical Activity Scale
Pain Detect$_1$	0.97	Pain Detect$_1$
Pain Detect$_2$	0.96	Pain Detect$_2$
Pain Detect$_3$	0.95	Pain Detect$_3$
Pain Detect$_4$	0.86	Pain Detect$_4$
Pain Detect$_5$	0.88	Pain Detect$_5$
Pain Detect$_6$	0.91	Pain Detect$_6$
ADL Taxonomia	0.95	ADL Taxonomia

Conclusions: The digitalized HSQs on touch screen gave statistically comparable results to answers given on a paper version of the same HSQs. Use of electronic questionnaires gives a safer and more precise data collection due to direct registration of answers, and implementation as well as use of this freeware is feasible for patients

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SHORT FORM-36 (SF-36) AND EUROQOL-5 DIMENSION (EQ-5D) RESULTS FROM RANDOMIZED, DOUBLE-BLIND PHASE 3 STUDIES OF TAPENTADOL PROLONGED RELEASE (PR) IN PATIENTS WITH MODERATE TO SEVERE CHRONIC NOCICEPTIVE AND NEUROPATHIC PAIN

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Purpose: To summarize SF-36 and EQ-5D health survey results from four 15-week, double-blind phase 3 studies of tapentadol PR in patients with osteoarthritis (OA) pain (NCT00421928 [OA study 1] and NCT00486811 [OA study 2]), low back pain (NCT00449176), and pain related to diabetic peripheral neuropathy (DPN; NCT00455520).
Methods: In the OA and low back pain studies, patients received placebo, tapentadol PR (100-250 mg bid), or oxycodone HCl controlled release (CR; 20-50 mg bid) during a 3-week titration period and a 12-week maintenance period. In the DPN study, patients received tapentadol PR (100-250 mg bid) during a 3-week open-label titration period; patients with at least a 1-point improvement in pain intensity (11-point numerical rating scale [NRS]) were randomized to receive placebo or their optimal dose of tapentadol PR (determined in the titration period) during a 12-week double-blind maintenance period. SF-36 and EQ-5D health survey questionnaires were used to assess health status. The SF-36 consists of 8 dimensions (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) measured on a 0 to 100 NRS (0 = being in poor health to 100 = being in good health) and summarized as physical component and mental component summaries. The EQ-5D consists of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), which are measured using 3 possible levels ("no problems," "some problems," and "extreme problems") and summarized

an overall EQ-5D health status index score. SF-36 and EQ-5D data from the 2 OA studies and the low back pain study were also pooled for analysis; comparisons versus placebo were prespecified.

Results: The intent-to-treat populations contained the following numbers of patients: low back pain study, n = 965; OA study 1, n = 1023; OA study 2, n = 987; DPN study, n = 389; pooled analysis, n = 2968. In the low back pain study and OA study 1, mean changes in SF-36 scores from baseline to endpoint were statistically significant for tapentadol PR compared with placebo for physical functioning, role-physical, bodily pain, and the physical component summary scores ($P \leq 0.029$ for all comparisons). In OA study 2, numerically greater improvements were observed with tapentadol PR compared with placebo for the SF-36 physical functioning, bodily pain, social functioning, role-emotional, and physical component summary scores. In the DPN study, mean changes in SF-36 scores from baseline to endpoint were statistically significant for tapentadol PR compared with placebo for role-physical, bodily pain, social functioning, and physical component summary scores (all $P \leq 0.012$). In the pooled analysis of SF-36 data from the 2 OA studies and the low back pain study, significant improvements were observed for tapentadol PR compared with placebo for physical functioning ($P < 0.001$), role-physical ($P = 0.001$), bodily pain ($P < 0.001$), vitality ($P = 0.041$), and physical component summary ($P < 0.001$) scores; no significant improvements were observed for oxycodone CR compared with placebo. In the low back pain study, OA study 1, and the DPN study, significantly greater improvements from baseline to endpoint were observed in the EQ-5D health status index score with tapentadol PR compared with placebo (all $P \leq 0.020$). In the pooled analysis of EQ-5D data from the 2 OA studies and the low back pain study, a significantly greater improvement from baseline to endpoint in the EQ-5D health status index score was seen with tapentadol PR compared with placebo ($P < 0.001$) and compared with oxycodone CR ($P < 0.001$); a significant improvement was not observed for oxycodone CR compared with placebo.

Conclusions: Treatment with tapentadol PR (100-250 mg bid) was associated with significant improvements in overall health and physical health status compared with placebo across nociceptive and neuropathic pain conditions.

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ASSESSMENT OF OPIOID WITHDRAWAL IN PATIENTS TREATED WITH TAPENTADOL PROLONGED RELEASE DURING AN OPEN-LABEL EXTENSION STUDY

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Purpose: Opioid withdrawal following treatment with tapentadol prolonged release (PR) was evaluated in this 1-year open-label extension study (ClinicalTrials.gov Identifier: NCT00487435).

Methods: Patients were eligible for enrollment if they completed 1 of 4 phase 3 studies: two 15-week studies that evaluated the efficacy of tapentadol PR and oxycodone controlled release (CR) compared with placebo for chronic osteoarthritis pain (NCT00421928) or low back pain (NCT00449176), a crossover study (two 2-week periods following a 3-week titration with tapentadol immediate release) to assess dose conversion between the immediate-release and prolonged-release tapentadol formulations in patients with chronic low back pain (NCT00594516), or a 1-year controlled long-term safety study of tapentadol PR and oxycodone CR in patients with chronic osteoarthritis or low back pain (NCT00361504). Patients who successfully completed one of the efficacy or crossover studies or who received oxycodone CR in the 1-year safety study were titrated to their optimal therapeutic dose of tapentadol PR (100-250 mg bid) during a titration period of up to 4 weeks then continued on their optimal dose for up to 48 weeks during the maintenance period. Patients who received tapentadol PR in the 1-year safety study continued on their optimal dose determined in the parent study. The Clinical Opiate Withdrawal Scale (COWS; 11-item scale scored from 0-48; <5 = no withdrawal, 5-12 = mild, 13-24 = moderate, 25-36 = moderately severe, and >36 = severe) and the Subjective Opiate Withdrawal Scale (SOWS; 15-item scale, possible score of 0-60; 60 = severe withdrawal) were used to assess opioid withdrawal in patients who did not take opioids after study drug discontinuation. COWS and SOWS scores were summarized according to the time of the last study drug intake. For the COWS, the categories were ≥2 days to <5 days and ≥5 days, and for the SOWS, the categories were 1, 2, 3, 4, and ≥5 days. Treatment-emergent adverse events (TEAEs) were recorded throughout the study.

Results: Of the 384 patients who had a COWS assessment from ≥2 to <5 days after study drug discontinuation, 88.8%, 10.7%, and 0.5% experienced no withdrawal, mild withdrawal, or moderate withdrawal, respectively. Of the 321 patients who had a COWS assessment ≥5 days after discontinuation of tapentadol PR, 90.7% had no withdrawal; mild and moderate withdrawal were observed in 8.7% and 0.6% of these patients, respectively. Based on results of COWS assessments, no patients experienced moderately severe or severe withdrawal. Mean (standard deviation) SOWS scores were as follows: 1 day (n = 2), 4.5 (2.12); 2 days (n = 536), 8.8 (9.48); 3 days (n = 556), 9.3 (9.99); 4 days (n = 561), 7.8 (9.24); ≥5 days (n = 552), 5.6 (7.20); mean SOWS scores for all time periods were low (<10), indicating minimal opioid withdrawal. The most common TEAEs (reported by ≥10% of patients [N = 1154]) were headache (13.1%), nausea (11.8%), and constipation (11.1%).

Conclusions: Results of COWS assessments completed by investigators ≥2 to <5 days following study drug discontinuation indicate that the majority of patients experienced no opioid withdrawal. SOWS assessments completed by patients each day immediately following study drug discontinuation also indicate a low incidence of withdrawal and suggest that opioid withdrawal peaks between Days 3 and 5. These results are similar to those shown previously following tapentadol PR treatment and are similar to those shown for placebo in previous placebo-controlled studies of tapentadol PR for chronic pain. Together, these results indicate that long-term treatment with tapentadol PR (100-250 mg bid) for up to 1 year in this open-label extension trial was associated with a low incidence of opioid withdrawal following treatment discontinuation without tapering in patients with moderate to severe chronic painful osteoarthritis or chronic low back pain.

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TREATMENT OF CARTILAGE DEFECTS IN THE KNEE USING ALGINATE BEADS CONTAINING HUMAN MATURE ALLOGENIC CHONDROCYTES: CLINICAL RESULTS AT 3 YEARS OF FOLLOW-UP

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Aim: The present study was designed to evaluate the implantation of alginate beads containing human mature allogenic chondrocytes for the treatment of symptomatic cartilage defects in the knee.

Methods: A biodegradable, alginate-based biocompatible scaffold containing human mature allogenic chondrocytes was used for the treatment of chondral and osteochondral lesions in the knee. Twenty-one patients were clinically prospectively evaluated with use of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and a Visual Analogue Scale (VAS) for pain preoperatively and at 3, 6, 9, 12, 24 and 36 months of follow-up.

Results: A statistically significant clinical improvement became apparent after 6 months and patients continued to improve during the 36 months of follow-up. Adverse reactions to the alginate/fibrin matrix seeded with the allogenic cartilage cells were not observed. Two of the procedures failed. One of the patients had loosening of the periosteal flap, which was attributed to a failure of the surgical procedure. The other failure case was the result of the poor quality and quantity of the repair tissue itself.

Discussion: The results of this pilot study show that the alginate-based scaffold containing human mature allogenic chondrocytes is feasible for the treatment of symptomatic cartilage defects in the knee. The described technique provides clinical outcomes equal to those of other cartilage repair techniques.